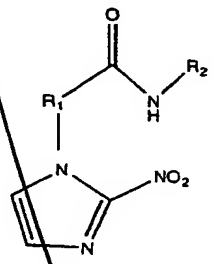
CLAIMS

1. A [^{18}F]-labelled perfluorinated-nitroaromatic compound having the formula:



wherein R_1 is CH_2 and R_2 is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula $CHXCX_2\ CY_3$ where X is halogen or hydrogen and Y is fluorine.

2. A compound according to claim 1 having specific radioactivity of the compound comprised between 1 and 30 Ci/mmol, preferably between 1 and 20 Ci/mmol, preferably between 1 and 10 Ci/mmol.

3. A compound according to claim 1 or 2 having the formula 2-(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl) acetamide ([^{18}F]-EF3).

4. A compound according to claim 1 or 2 having the formula 2(2-nitro-1H-imidazol-1-yl)-N-(2,2,3,3,3-pentafluoropropyl) acetamide ([^{18}F]-EF5).

5. A method for the synthesis of a compound according to one of the claims 1-4, comprising the step of coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [^{18}F]-labelled perfluoroalkyl amine derivative.

6. A method according to claim 5, wherein said coupling is a classical peptide coupling using a derivative of 2-(2-nitro-imidazol-1-yl) acetic acid in which the OH group of the carboxyl function has been replaced by a good leaving group.

7. A method for the synthesis of a compound according to of one of the claims 1-4 or the corresponding non-labelled form thereof, comprising the steps of:

a) adding a THF solution of 2 of Figure 7 to a suspension of PYBOP in THF followed by Et_3N,

b) adding an amine 1 of Figure 7 and Et_3N to the solution obtained in step (a),

c) adding a catalytic amount to the solution obtained in step (b) of pTsOH and refluxing the solution,

d) cooling the solution obtained after step (c) at ambient temperature and adding a sodium bicarbonate solution,

e) extracting the product obtained after step (d) with ethyl acetate and drying and concentrating the product with ethyl acetate,

f) purifying the residue obtained after step (e) by column chromatography on silica gel,

g) removing traces of water by washing the product of step (f) with trifluoroacetic anhydride,

h) reacting said persulphurated derivative obtained from step (g) with a suitable labelled or non-labelled perfluorinating agent and a suitable oxidant resulting in a compound having a high yield of fluor atom incorporation,

i) deprotecting the nitrogen function, resulting in a perfluoroalkyl amine derivative, and

j) coupling the perfluoroalkyl amine derivative obtained in step (i) with an activated form of 2-(2-nitro-imidazol-1-yl) acetic acid, resulting in the [^{18}F]-labelled or non-labelled perfluorinated-nitroaromatic compound.

8. A method according to claim 7 wherein hydrogen fluoride/pyridine complex (HF-Pyridine) is used as a perfluorinating agent and 1,3-dibromo-5,5-dimethylhydantoin (DBH) is used as an oxidant resulting in a compound having a high yield of fluor atom incorporation.

9. A [^{18}F]-labelled compound obtainable by a method according to one of the claims 5, 6, 7 or 8.

10. A first intermediate compound having the general formula of an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group and wherein the carboxyl function has been transformed into a dithioester function or a synthetically equivalent persulphurated moiety.

11. A first intermediate compound according to claim 10, wherein the imido group is a phthalimido group.

12. A first intermediate compound according to claim 10 or 11, obtainable via steps a to g of the method as claimed in claim 7.

13. A first intermediate compound according to claim 10, 11 or 12, being ethyl 3-(N-phthalimido)-aminopropanedithioate, N-(3,3,3-trifluoro-2-thioxopropyl) phthalimide, N-{[2-(trifluoromethyl)-1,3-dithiolan-2-yl] methyl} phthalimide, methyl (or ethyl) 3-phthalimide-2,2-difluoropropanedithioate, N-[2,2-difluoro-3,3,3-tris(methylthio) propyl] phthalimide or N-[2,2-difluoro-3,3,3-tris(ethylthio)propyl] phthalimide.

14. A second intermediate compound having the general formula of a [^{18}F]-labelled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group.

15. A second intermediate compound according to claim 14, wherein the imido group is a phthalimido group.

16. A second intermediate compound according to claim 14 or 15, obtainable via steps a to h of the method as claimed in claim 7 or 8.

17. A second intermediate compound according to claim 14, 15 or 16, being N-(3,3,3-trifluoropropyl)phthalimide.

18. A third intermediate compound having the general formula of a [^{18}F]-labelled perfluoroalkyl amine.

19. A third intermediate compound according to claim 18, being [^{18}F]-labelled 3,3,3-trifluoropropyl amine.

20. A third intermediate [^{18}F]-labelled compound obtainable via steps a to i of the method as claimed in claim 7 or 8.

21. Use of a compound according to one of the claims 1-4 as bioactive compound.

22. A [^{18}F] labelled bioactive compound synthesized using as intermediates a first intermediate as claimed in one of the claims 10-13, a second intermediate as claimed in one of the claims 14-17 and a third intermediate as claimed in one of the claims 10-13.

23. A [^{18}F] labelled bioactive compound synthesized using as intermediates a first intermediate as claimed in one of the claims 10-13.

24. Method of perfuorination using as an intermediate a compound as claimed in one of the claims 10-13.

25. The compound of claim 22 which is an [^{18}F] labelled perfluorinated nitroimidazole compound having an incorporation of [^{18}F] atoms characterized by a specific radioactivity of the compound comprised between 1 and 30 Ci/mmol, preferably between 1 and 20 Ci/mmol, preferably 1 and 10 Ci/mmol.

26. A method for the detection of tissue hypoxia in a patient comprising:
- introducing an [^{18}F] labelled nitroimidazole compound of any of claims 1 to 4 into said patient,
- imaging tissue hypoxia in said patient, and
- quantifying tissue hypoxia in said patient.

27. A method according to claim 26 wherein the detection technique used in said method is positron emission tomography.

28. A method for the detection of tissue hypoxia in a tissue comprising:
- introducing an [^{18}F] labelled nitroimidazole compound of any of claims 1 to 4 into a patient,
- removing a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

29. A method for the detection of an [^{18}F] labelled bioactive compound in a patient comprising:
- introducing an [^{18}F] labelled bioactive compound according to claim 1-4 into said patient,
- imaging the presence of said [^{18}F] labelled bioactive compound in said patient, and
- optionally, quantifying the presence of said [^{18}F] labelled bioactive compound in said patient.

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30. A method for the detection of [^{18}F] labelled bioactive compound in a tissue comprising:

- introducing an [^{18}F] labelled bioactive compound of claim 1-4 into a patient,
- taking a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

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